

REMARKS

The present communication is responsive to the Official Action mailed May 31, 2006. Entry of the foregoing and reexamination and reconsideration of the above-captioned application pursuant to and consistent with 37 C.F.R. § 1.112 and in light of the amendments and remarks that follow are respectfully requested.

Applicant has amended the specification to correct minor typographical errors and omissions. No new matter has been added by way of these amendments.

Claims 18-38 stand rejected. Claims 22-38 have been amended and claims 18-21 have been cancelled without prejudice or disclaimer to the filing of continuing applications relating to same. In addition, claims 39-55 are newly added, support for which is found throughout the specification. No new matter has been added by way of these amendments to the claims.

35 U.S.C. § 112 ¶1 (Written Description)

Claims 20 and 21 are rejected for allegedly lacking a written description. Claims 20 and 21 have been cancelled without prejudice or disclaimer, and therefore the rejection as to those claims is now moot.

35 U.S.C. § 112 ¶1 (Enablement)

Claims 18 and 20-38 have been rejected for allegedly failing to comply with the enablement requirement. The Examiner argues that "[i]n the instant case, the specification is not enabling based on \* \* \* quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art, unpredictability and the breadth of claims." Applicant respectfully traverses.

Claims 18-21 have been cancelled, thus, the rejection as to those claims is moot. Turning to claims 22-38, the proper standard in determining whether an invention has been enabled requires a determination of whether the disclosure is sufficient

to enable those skilled in the art to practice the claimed invention. Accordingly, the specification need not disclose what is well-known in the art. In the field of cosmetological and dermopharmaceutical sciences, there exists a high level of skill in the art such that a skilled artisan would not require undue experimentation in arriving at the claimed compositions of the present invention or practicing the claimed methods of use. In view of the synthesis experiment of Example No. 1, disclosed at [0089] - [0091], a skilled artisan would understand how to synthesize the products of the claimed compositions. Indeed, this type of chemical synthesis in view of the teachings of the application, is within the level of skill in the art.

In addition, a skilled artisan would be possessed with the requisite knowledge to prepare the cosmetic and dermopharmaceutical compositions comprising the instant compounds of formula I in combination with other active substances and principal adjuvants in view of the specification's teachings. Specifically, Examples 2 - 4 at [0092] - [0095] teach, by way of illustration, combinations of the claimed compound with a carrier, or active substance, or a principal adjuvant. Together with the teachings in the specification describing suitable carriers, active substances and principal adjuvants, a skilled artisan could certainly prepare the claimed cosmetic and dermopharmaceutical compositions and expect a predictable result with regard to the efficacy of the composition for its intended purpose(s).

Method claims 37 and 38 are also rejected for lack of enablement. The Examiner argued that "there is no teaching or guidance how the instant compounds will decrease pigmentation (where melanin pigment is already formed), slim, reduce cellulite or firm the skin of a person." The Examiner also argued that there were no working examples showing efficacy in animal models, no teaching showing the well-known utility of

structurally related compounds, and that it would require undue experimentation to demonstrate the efficacy of instant compounds of formula I in combination with active substances for use in the dermatological conditions of claims 37 and 38. Applicant respectfully traverses.

With regard to claim 37, the specification teaches a skilled artisan how to successfully make and use the invention. Specifically, Example No. 2 at [0092] – [0093] provides a topical formulation for a day cream and emulsion used "to lighten and moisturize face and skin". In addition, paragraph [0048], for example, teaches the required concentration ranges for using the invention. Certainly, *in vitro* studies on the human cell line in Example No. 5 are sufficient to support the method of claim 37. Finally, the Applicant even provides Example No. 5 and strong positive data (Fig. 1) to illustrate a working embodiment of the invention.

With regard to claim 38, Example Nos. 3 – 4 teach formulations for making and using the topical skin formulations, namely, slimming gels and creams. In addition, concentration ranges for using the invention are provided at paragraph [0048]. Furthermore, Example Nos. 6 – 7 illustrate that the claimed compositions of the present application can, in fact, be used to inhibit lipogenesis and inhibit lipid peroxidation, which supports the notion that the composition is effective for its intended purpose(s) – slimming, reducing cellulite or firming skin. Certainly, *in vitro* studies on the cell lines in Example Nos. 6 – 7 are sufficient to support the method of claim 38.

35 U.S.C. § 112 ¶2 (Indefiniteness)

Claims 19-22, 26, 29-32, and 34-38 are rejected as being indefinite. The Examiner made several rejections each of which is addressed below:

- "Claim 19 does not end with a period."

Claim 19 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot.

- "In claim 20, steps for extracting compounds of formula I from *glacium flavum* are missing."

Claim 20 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot.

- "In claim 21, steps for preparing compounds of formula I are missing. It is not clear what are the reactants, starting materials, etc."

Claim 21 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot.

- "In claims 22, 37 and 38, the terms---active substance or principal adjuvant---is indefinite since specific substance or adjuvant is not defined."

In this regard, the terms "active substance" and "principal adjuvant" are well-defined in the specification. Specifically, "active substance" appears in the specification at [0067], [0081], and [0083] and again at claim 30. "Principal adjuvant" is discussed at [0056], [0066], and [0067] and again at claim 29.

- "In claim 26, the term---other inorganic support---is indefinite since it is not defined."

Applicant respectfully points the Examiner's attention to paragraph [0084] for examples of "inorganic support" for use in accordance with the present disclosure.

- "In claims 29 and 30, specific substances, actives and agents are not defined."

Claims 29 and 30 each set forth and circumscribe the particular principal adjuvants and active substances with a reasonable degree of clarity and particularity such that a skilled artisan could interpret the metes and bounds of the claimed invention(s). In addition, the specification teaches at paragraphs [0056] and [0067] some of the principal adjuvants

that can be used in accordance with the present disclosure. Some examples of active substances are disclosed at paragraphs [0081] - [0084].

o "In claims 31, 32 and 34-36, specific plant extract is not defined."

"Plant extract" is described in the specification and its interpretation is broader than an extract only from the *glaucium flavum* plant. The extract of the *glaucium flavum* is but one example of a plant extract for use in the present invention. In another example, the specification at [0041] discloses the appropriate plants for use, in the case of a plant from the vegetable origin. As such, a skilled artisan formulating topical skin cosmetic and dermopharmaceutical compositions containing plant extracts would understand the metes and bounds of the claim.

With regard to each of the above rejections for allegedly failing to comply with the definiteness requirement of 35 U.S.C. § 112 ¶2, Applicant respectfully submits that in view of the foregoing, the claims are as clear and definite as the subject matter will allow and certainly would not be indefinite to a person of ordinary skill in the art. Accordingly, withdrawal of the foregoing rejections is earnestly solicited.

35 U.S.C. § 102 (a) (Novelty)

In general, the claims have been rejected as being allegedly anticipated by the following cited references under 102(a).

Su et al. (US Patent 6,313,134)

Claims 18 and 21-36 have been rejected as being allegedly anticipated by Su et al. (US 6,313,134) (hereinafter "Su"). The Examiner argues that Su discloses uses of Thaliporphine derivatives and pharmaceutical compositions containing these compounds for the treatment of cardiac diseases. Claims 18 and 21 have been cancelled without

prejudice or disclaimer, and therefore the rejection as to those claims is moot. Claims 22-36, however, have been amended to more clearly distinguish over a pharmaceutical composition, as in Su, that is "to be administered orally or by injection to a patient in need." (Col. 5, l. 3.) Rather, the amended claims at issue are drawn to topical cosmetic or dermatological compositions useful for topical administration. As such, withdrawal of this rejection is requested.

Lintner (WO 02/066000)

Claims 22-38 have been rejected as being anticipated by Lintner. The Examiner argues that Lintner disclosed cosmetic compositions containing Boldine for treating excess weight, cellulite and skin toning. This rejection is not proper because § 102 (a) requires that the "art" in question be of "another". As the Lintner of the art is the same as the present inventor, WO/066000 does not qualify as prior art. In addition, independent claim 22 (drawn to a topical composition) and independent claim 38 (drawn to a method of slimming, reducing cellulite or firming the skin) have been amended to exclude Boldine [2,9-dihydroxy-1,10-dimethoxy-6-methyl-noraporphine (formula I,  $R^1 = H$ ,  $R^2 = R^3 = CH_3$ ,  $R^4 = H$ ,  $R^5 = CH_3$ )]. Accordingly, claims 22 and 38, as well as the dependent claims stemming from base claim 22 (e.g., claims 23-36) should now be in condition for allowance over Lintner.

Turning to claim 37, nothing in the art of record teaches or suggests the use of Boldine for decreasing pigmentation. We respectfully request that the rejection of claims 22-38 in view of Lintner be withdrawn therefor.

Pauly (EP 1145709)

Claims 22-36 have been rejected as being anticipated by Pauly. The Examiner argues that Pauly discloses natural products for cosmetic compositions containing Boldine. As discussed above, independent claim 22 is now drawn to a topical

composition which excludes Boldine [2,9-dihydroxy-1,10-dimethoxy-6-methyl-noraporphine (formula I,  $R^1 = H$ ,  $R^2 = R^3 = CH_3$ ,  $R^4 = H$ ,  $R^5 = CH_3$ )]. Accordingly, claim 22 is not anticipated and dependent claims stemming from base claim 22 (e.g., claims 23-36) should now be in condition for allowance. We respectfully request that the rejection of claims 22-38 in view of Pauly be withdrawn.

35 U.S.C. § 102 (b) (Novelty)

In general, the claims have been rejected as being allegedly anticipated by the following cited references under 102(b).

Krell (WO 99/16441)

Claims 18 and 21-36 have been rejected as being anticipated by Krell. The Examiner argues that Krell discloses Aporphinoid compounds (Boldine, Glaucine and Examples 30-40 on pages 13-14) and pharmaceutical compositions for treating MMP-mediated diseases. Claims 18 and 21 have been cancelled without prejudice or disclaimer, and therefore the rejection as to those claims is moot. Claims 22-36, however, have been amended to more clearly distinguish over a pharmaceutical composition, as in Krell, that is to be "administered enterally or parenterally in a liquid or solid form." (Page 15, ll. 11.) The amended claims at issue are now drawn to topical cosmetic or dermatological compositions useful for topical administration. Nothing in the art of record anticipates claims drawn to topical cosmetic or dermopharmaceutical compositions as recited in amended claim 22, which are useful for topical administration. Accordingly, withdrawal of this rejection is respectfully requested.

Nizard (WO 00/59466)

Claims 22-36 have been rejected as being anticipated by Nizard. The Examiner argues that Nizard discloses cosmetic compositions comprising Boldine. As discussed above,

independent claim 22 is now drawn to a topical composition which excludes Boldine [2,9-dihydroxy-1,10-dimethoxy-6-methyl-noraporphine (formula I, R<sup>1</sup> = H, R<sup>2</sup> = R<sup>3</sup> = CH<sub>3</sub>, R<sup>4</sup> = H, R<sup>5</sup> = CH<sub>3</sub>)]. Accordingly, dependent claims stemming from base claim 22 (e.g., claims 23-36) should now be in condition for allowance. We respectfully request that the rejection of claims 22-36 in view of Nizard be withdrawn.

Maasbol (U.S. Patent 4,279,914)

Claims 18, 22 and 24-36 have been rejected as being anticipated by Maasbol. The Examiner argues that Maasbol discloses compositions and methods for inhibition of Thrombocyte aggregation. Claim 18 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot. Claims 22 and 24-36, however, have been amended to more clearly distinguish over a pharmaceutical composition, as in Maasbol, that is to be administered in an "oral dosage unit form" or "in form of a pill, dragee, tablet, or capsule" or as an injection (See Col. 8, ll. 56-67). The amended claims at issue are now drawn to topical cosmetic or dermatological compositions useful for topical administration. Nothing in the art of record anticipates claims drawn to topical cosmetic or dermopharmaceutical compositions as recited in amended claim 22, which are useful for topical administration. Accordingly, withdrawal of this rejection is respectfully requested.

Cortes (Journal of Natural Products)

Claims 18 and 19 have been rejected as being anticipated by Cortes. The Examiner argues that Cortes discloses noraporphine compounds. Claims 18 and 19 have been cancelled without prejudice or disclaimer, and therefore the rejection as to those claims is moot.

Hoshino (Chem. Pharm. Bull.)

Claims 18 and 19 have been rejected as being anticipated by Hoshino. The Examiner argues that Hoshino

discloses studies on tetrahydroisoquinolines. Claims 18 and 19 have been cancelled without prejudice or disclaimer, and therefore the rejection as to those claims is moot.

Chen (Planta Medica)

Claim 18 has been rejected as being anticipated by Chen. The Examiner argues that Chen discloses Antiplatelet and vasorelaxing actions of some aporphinoids. Claim 18 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot.

Yu (Biochem Journal)

Claim 18 has been rejected as being anticipated by Yu. The Examiner argues that Yu discloses inhibition of nitric oxide synthase by Thaliporphine. Claim 18 has been cancelled without prejudice or disclaimer, and therefore the rejection is moot.

In addition to the foregoing remarks and in view of the amendment to claim 22 as described above, allowance of new claims 48 and 49 and dependent claims 50-54 is earnestly solicited. New claims 48 and 49 include the limitations of amended claim 22. Specifically, new claim 48 recites that the compound of formula I is 1,2,9,10-tetramethoxy-6-methyl-noraporphine (formula I,  $R^1 = R^2 = R^3 = R^4 = R^5 = CH_3$ ), support for which is found at paragraphs [0041] and [0045] – [0047], for example. New claim 49 recites that the compound of formula I is 2,9-diacetyloxy-1,10-dimethoxy-6-methyl-noraporphine (formula I,  $R^1 = R^4 = -COCH_3$ ,  $R^2 = R^3 = CH_3$ ,  $R^5 = CH_3$ ), support for which is found at paragraphs [0039] and [0089] – [0119], for example. Additional limitations to claims 48 and 49 are recited in new claims 50-54, support for which is found throughout the application. Accordingly, allowance of claims 48-54 is respectfully requested.

Should the Examiner have any questions with regard to the foregoing, the Examiner should contact applicant's attorney

at the Examiner's convenience at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

From the foregoing, further and favorable action in the form of a notice of allowance is believed to be next in order and such action is earnestly solicited.

Dated: October 2, 2006

Respectfully submitted,

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